REMARKS

Per Applicants' election of species filed August 19, 2003, Applicants have cancelled claims 6 and 13, and will pursue these claims in a subsequent filing. The Applicants will now address the Examiners' rejections in the order presented in the office action.

Claim Rejections-35 USC 112, 1st paragraph

Claims 1-2, 8, 9, 15, 16 stand rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner has rejected the claims because they encompass a genus of viral vectors with the properties described by the Applicants, whereas the Examiner believes that the specification provides sufficient description of adenoviral vectors. The Examiner will note that the claims as amended claim adenovirus. Thus, the rejection should be obviated.

Claims 1-5, 7-10, 15, and 16 also stand rejected under 35 USC 112, 1st paragraph for lack of enablement. Specifically, the Examiner has stated that Applicants' claims are enabled for an adenovirus vector comprising an E2F responsive promoter operably linked to an adenovirus immediate early gene. The Examiner will note that Applicants have amended the claims to recite "early gene" rather than "immediate early gene." Applicants believe that a skilled practitioner of this art would have no trouble constructing adenoviral vectors where an E2F responsive promoter is operably linked to adenoviral genes other than E1a. Indeed, Applicants describe such vectors where an E2F responsive promoter is operably

linked to the E4 gene. Thus, Applicants respectfully submit that the rejection is overly broad and should be withdrawn.

The Examiner has rejected claim 16 in part because it reads on an in vivo method of treating cancer, and theExaminer has cited various references which stand for the proposition that viral gene therapy may give unpredictable results. None of these references, however, show experiments using the type of adenoviral vectors described and claimed by the Applicants. Thus, absent such references to support the rejection, Applicants' specification is presumed to be enabled, and the rejection should be withdrawn.

35 USC 102 Rejection

Claims 1-5, 7-12, 14-16 stand rejected as being anticipated by Yu (US2001/005333352).

Suffice it to say that Applicants have amended the claims to recite that their adenoviral vectors have a mutation in the E1a region of the vectors, which mutation causes a loss of RB binding to the protein encoded by the E1a region. This newly claimed aspect of Applicants' invention is not shown by Yu, and thus the rejection premised thereon should be withdrawn.

35 USC 103(a) Rejection

Claims 1-5, 7-12, and 14-16 stand rejected under 103(a) as being unpatentable over with Hallenbeck (US Pat. No. 5, 998, 205) or Gregory (US 2003/0026789), taken with Fine (WO/ 98/13508).

Two features of Applicants' claimed invention are neither shown nor suggested by Hallenbeck, or Gregory. As the Examiner has noted, neither Hallenbeck nor Gregory show or suggest an E2F responsive promoter used by the Applicants. Moreover, neither of these references show or suggest a newly

amended aspect of Applicants' invention which is that the adenoviral vector has a mutation in the E1a region of the vector, which mutation causes a loss of RB binding to the protein encoded by the E1a region. Thus, it is respectfully submitted that since neither reference shows these aspects of Applicants' claimed invention, the primary references fail to support a 103 rejection.

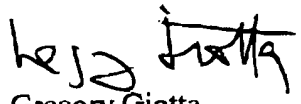
With regard to Fine, Applicants submit that this reference supports the unobviousness of their invention, and provides no motivation to employ an E2F responsive promoter in the context of Applicants' invention. Fine employs and E2F promoter to drive the expression of a toxic heterologous gene. Clearly, if Applicants' invention were obvious, Fine would have used the E2F promoter to drive the expression of an adenovirus early gene, which he did not.

If the Examiner has any questions with regard to this amendment, the Examiner is encouraged to call the undersigned at: 510:262-8710.

The Commissioner is authorized to charge any fees associated with this communication, to Deposit Account No. 15-0615 for any matter in connection with this response, including a 3 month extension of time fee, which may be required A Petition for a Three Month Extension of Time accompanies this Response.

Respectfully submitted,

Date: September 17, 2003

By: 
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APPENDIX A
PENDING CLAIMS AFTER INSTANT AMENDMENT

Claim 1 (Amended). An adenoviral vector comprising an E2F responsive transcriptional nucleotide regulatory site that controls the expression of an early adenoviral gene, and a mutation in the E1a region of said adenoviral vector, which mutation causes a loss of RB binding to the protein encoded by the E1a region.

Claims 2 – 3 - Canceled

Claim 4 (Amended). An adenoviral vector as described in claim 1, wherein said transcriptional nucleotide regulatory site is a promoter.

Claim 5 (Amended). An adenoviral vector as described in claim 4, wherein said E2F responsive promoter is substituted for an endogenous adenoviral E1a promoter.

Claim 6 - Canceled

Claim 7 (Amended). An adenoviral vector as described in claim 5, wherein said viral vector further comprises nucleotide regulatory sites that substantially facilitate viral replication comprising Sp1, ATF, NF1 and NFIII/Oct-1.

Claim 8 (Amended). An adenoviral vector comprising a viral transcriptional nucleotide regulatory site that controls the expression of an early adenoviral gene, wherein said site is inactivated by the insertion of an E2F responsive transcriptional nucleotide regulatory site such that said E2F responsive transcriptional nucleotide regulatory site controls the expression of said viral gene, and said adenoviral vector further comprises a mutation in the E1a region of, which mutation causes a loss of RB binding to the protein encoded by the E1a region.

Claims 9 – 10 Canceled

Claim 11 (Amended). An adenoviral vector as described in claim 8, wherein said inactivated transcriptional nucleotide regulatory site is a promoter.

Claim 12 (Amended). An adenoviral vector as described in claim 11, wherein said inactivated transcriptional nucleotide regulatory site is an endogenous adenoviral E1a promoter.

Claim 13 - Canceled.

Claim 14 (Amended). An adenoviral vector as described in claim 11, wherein said inactivated transcriptional nucleotide regulatory site comprises both an endogenous adenoviral E1a and E4 promoters.

Claim 15 (Canceled) An adenoviral vector as described in claims 1 or 8, wherein said transcriptional nucleotide regulatory sequence that is E2F responsive is human E2F-1.

Claim 16 (Canceled). A method for killing cancer cells in the presence of normal cells, comprising the steps of: contacting under infective conditions (1) an adenoviral vector as described in claims 1 or 8 with (2) a cell population

comprising cancer and normal cells, and allowing sufficient time for said adenovirus to infect said cell population.